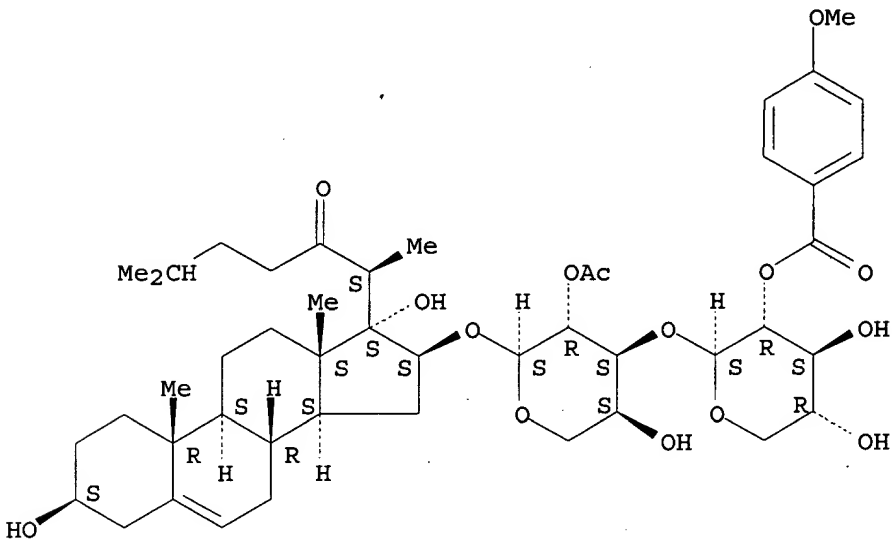
```
=> d his

     (FILE 'HOME' ENTERED AT 15:27:28 ON 01 NOV 2006)

     FILE 'REGISTRY' ENTERED AT 15:27:45 ON 01 NOV 2006
L1                STRUCTURE UPLOADED
L2              0 S L1 SSS SAM
L3              1 S L1 SSS FULL

     FILE 'CAPLUS, MEDLINE' ENTERED AT 15:29:22 ON 01 NOV 2006
L4              1 S L3
L5             66 S OSW-1
L6              4 S L5 AND APOPTOSIS
L7              2 S L5 AND PATIENT?
L8              0 S L5 AND ADMINISTER?
L9              0 S L5 AND ORAL?
L10             2 S L5 AND PANCREAT?
L11             1 S L5 AND CARCINOMA?
L12             1 S ?ORSAPONIN? (P) PANCREA?
```

```
=> d his

     (FILE 'HOME' ENTERED AT 15:27:28 ON 01 NOV 2006)

     FILE 'REGISTRY' ENTERED AT 15:27:45 ON 01 NOV 2006
L1                STRUCTURE UPLOADED
L2              0 S L1 SSS SAM
L3              1 S L1 SSS FULL

     FILE 'CAPLUS, MEDLINE' ENTERED AT 15:29:22 ON 01 NOV 2006
L4              1 S L3
L5             66 S OSW-1
L6              4 S L5 AND APOPTOSIS
L7              2 S L5 AND PATIENT?
L8              0 S L5 AND ADMINISTER?
L9              0 S L5 AND ORAL?
L10             2 S L5 AND PANCREAT?
L11             1 S L5 AND CARCINOMA?
L12             1 S ?ORSAPONIN? (P) PANCREA?
```

=> d scan

L4 1 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI)
MF C47 H68 O15

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

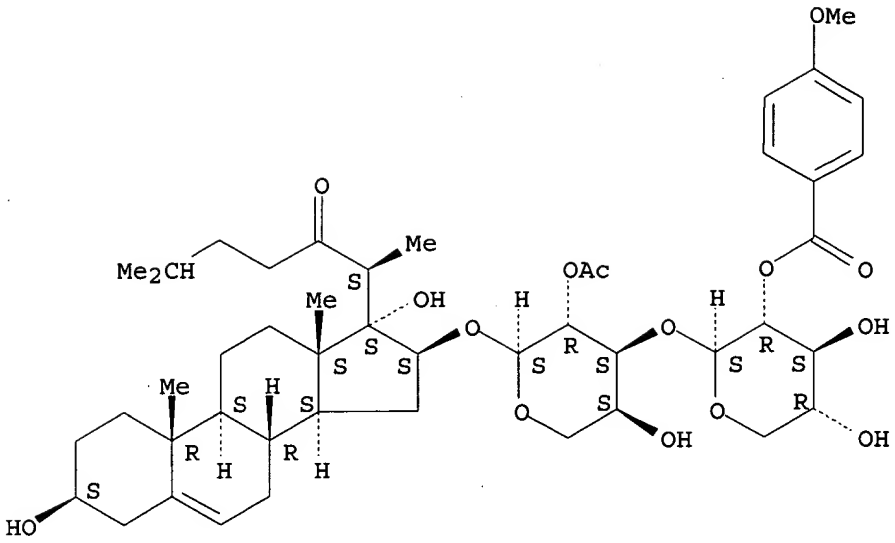
L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1300875 CAPLUS
DOCUMENT NUMBER: 144:425214
TITLE: OSW-1: a Natural Compound With Potent Anticancer Activity and a Novel Mechanism of Action
AUTHOR(S): Zhou, Yan; Garcia-Prieto, Celia; Carney, Dennis A.; Xu, Rui-Hua; Pelicano, Helene; Kang, Ying; Yu, Wensheng; Lou, Changgang; Kondo, Seiji; Liu, Jinsong; Harris, David M.; Estrov, Zeev; Keating, Michael J.; Jin, Zhendong; Huang, Peng
CORPORATE SOURCE: Departments of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of the National Cancer Institute (2005), 97(23), 1781-1785
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The naturally occurring compound 3β,16β,17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1 3)-(2-O-acetyl-α-L-arabinopyranoside) (OSW-1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concns. that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochem. analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro anal. revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.

IT 145075-81-6, OSW-1
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(OSW-1 damaged mitochondrial membrane and cristae, leading to loss of transmembrane potential, increased cytosolic calcium and activation of calcium-dependent apoptosis in both human leukemia tissue and in pancreatic cancer cell line)

RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902089 CAPLUS
DOCUMENT NUMBER: 141:395754
TITLE: Preparation of orsaponin [3β, 16β, 17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1->3)-(2-O-acetyl-α-L-arabinopyranoside)] and its derivatives for their use as cancer therapeutics
INVENTOR(S): Haung, Peng; Keating, Michael J.; Jin, Zhendong
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA; University of Iowa Research Foundation
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091484	A2	20041028	WO 2004-US10676	20040407
WO 2004091484	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005004044	A1	20050106	US 2004-819479	20040407
PRIORITY APPLN. INFO.:			US 2003-460946P P	20030407

OTHER SOURCE(S): MARPAT 141:395754
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

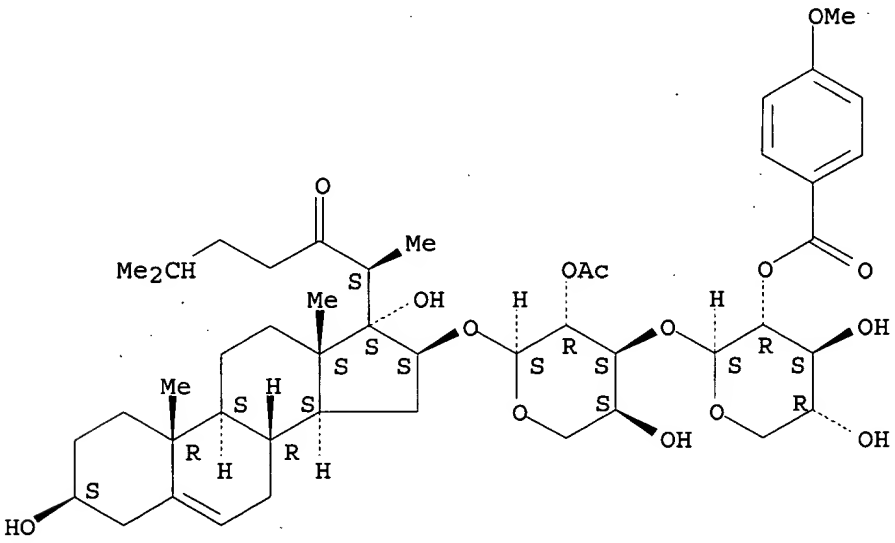
AB The present invention concerns methods for treating pancreatic cancers, leukemias, colon cancers, malignant gliomas and other brain tumors, and ovarian cancers which comprise providing to an individual compns. comprising an orsaponin or its derivs., such as I [R1 = H, OH, OMe; R2 = H, OH, ester, amide; R3, R4 = H, OH; R3R4 = double bond; R5 = H, disaccharide, monosaccharide, trisaccharide; R6 = disaccharide, monosaccharide, trisaccharide; R7, R8 = Me, alkyl; R9 = α-Me, β-Me]. The invention also provides processes and intermediates useful for preparing compds. of formula I and various therapeutically useful derivs. Thus, orsaponin (II) was prepared via a multistep reaction sequence starting from 5-pregnen-16α,17α-epoxy-3β-ol-20-one, 1,2,3,4-tetra-O-acetyl-L-arabinose, 4-methoxybenzoyl chloride and 1,2,3,4-tetra-O-acetyl-D-xylopyranose. II exhibited an IC50 = <0.1 nM in human leukemia cells (ML-1) and human lymphoma cells (Raji).

IT 145075-81-6P, Orsaponin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of orsaponin and its derivs. for their use as cancer therapeutics)

RN 145075-81-6 CAPLUS

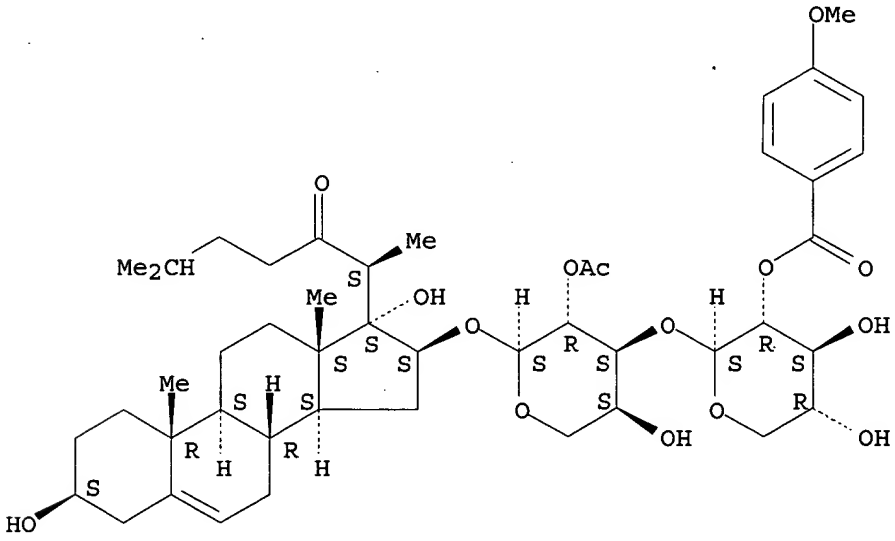
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:265320 CAPLUS
DOCUMENT NUMBER: 144:391258
TITLE: 1. Design and synthesis of carbohydrate cancer vaccines based on biochemical modification of cancer cells. 2. Studies on the total synthesis of an antitumor saponin, OSW-1
AUTHOR(S): Pan, Yanbin
CORPORATE SOURCE: Case Western Reserve Univ., Cleveland, OH, USA
SOURCE: (2005) 336 pp. Avail.: UMI, Order No. DA3176587 From: Diss. Abstr. Int., B 2005, 66(5), 2590
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT 145075-81-6P, OSW-1
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1 design and synthesis of carbohydrate cancer vaccines based on biochem. modification of cancer cells 2 studies on total synthesis of antitumor saponin, OSW-1)
RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1300875 CAPLUS
DOCUMENT NUMBER: 144:425214
TITLE: OSW-1: a Natural Compound With Potent Anticancer Activity and a Novel Mechanism of Action
AUTHOR(S): Zhou, Yan; Garcia-Prieto, Celia; Carney, Dennis A.; Xu, Rui-Hua; Pelicano, Helene; Kang, Ying; Yu, Wensheng; Lou, Changgang; Kondo, Seiji; Liu, Jinsong; Harris, David M.; Estrov, Zeev; Keating, Michael J.; Jin, Zhendong; Huang, Peng
CORPORATE SOURCE: Departments of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of the National Cancer Institute (2005),

97(23), 1781-1785
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

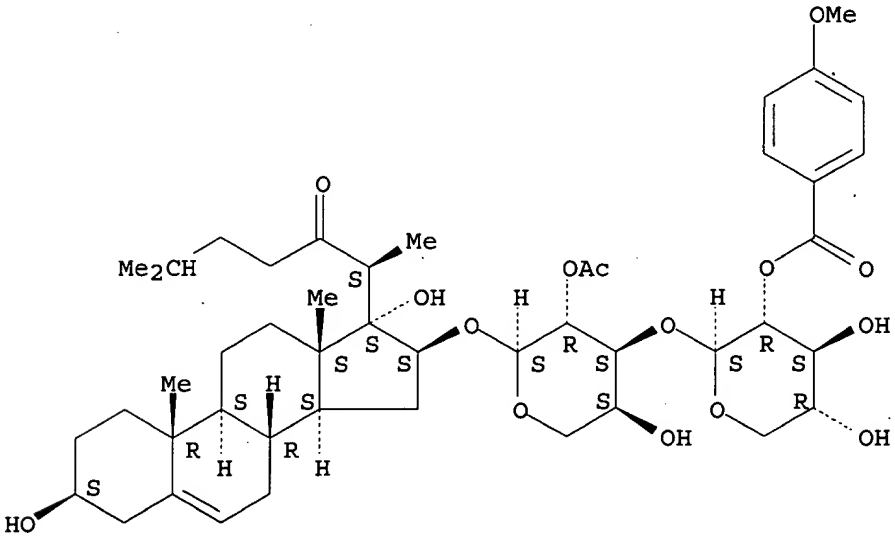
AB The naturally occurring compound 3β,16β,17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1 3)-(2-O-acetyl-α-L-arabinopyranoside) (OSW-1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concns. that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochem. analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro anal. revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.

IT 145075-81-6, OSW-1
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(OSW-1 damaged mitochondrial membrane and cristae, leading to loss of transmembrane potential, increased cytosolic calcium and activation of calcium-dependent apoptosis in both human leukemia tissue and in pancreatic cancer cell line)

RN 145075-81-6 CAPLUS

CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

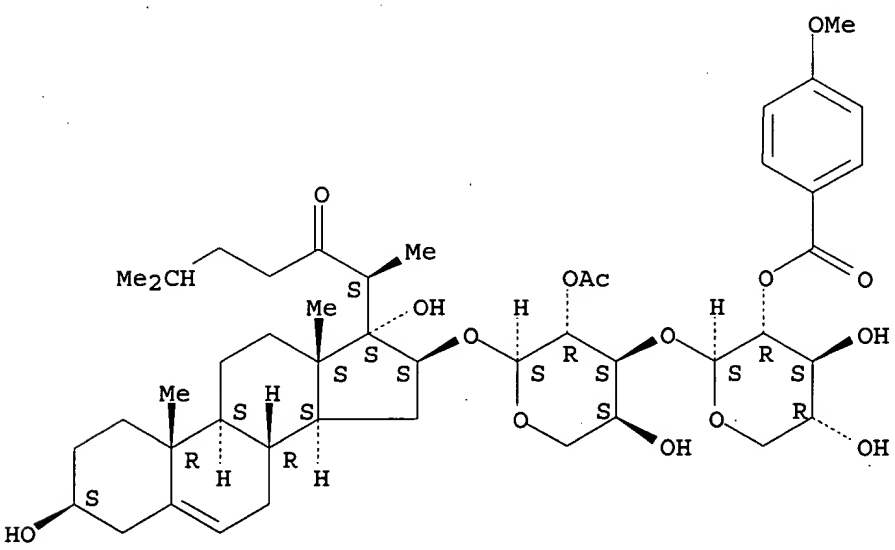
L7 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:593826 CAPLUS
DOCUMENT NUMBER: 143:120165
TITLE: Distribution of an antitumor natural product OSW-1 in ganglioside GM3-phospholipid membranes
AUTHOR(S): Yokoyama, Shoko; Ohtsuka, Isao; Takeda, Tadahiro; Sashida, Yutaka
CORPORATE SOURCE: Sch. Pharm. Sci., Kyushu Univ. Health Welfare, Nobeoka, 882-8508, Japan
SOURCE: Material Technology (Tokyo, Japan) (2005), 23(1), 54-58
CODEN: MTECFQ
PUBLISHER: Zairyo Gijutsu Kenkyu Kyokai
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The distribution of OSW-1 having antitumor activity, in L-α-dipalmitoylphosphatidylcholine (DPPC) and ganglioside GM3 (GM3) monolayers, was observed by atomic force microscopy (AFM). As a result, OSW-1 was not observed to be distributed in the DPPC monolayer, while it was distributed in the GM3 monolayer. Furthermore, a strongly attractive interaction between OSW-1 and GM3 was observed and thus the membrane structure of GM3 changed. In the mixed GM3/DPPC (2:8) monolayers, OSW-1 was distributed in the GM3-rich phase (percolation-pattern region) in the mixed membrane. The specific distribution of OSW-1 in the GM3 membranes and the strongly attractive interaction between OSW-1 and GM3 seem to be related to its potent activity against cancer cells.

IT 145075-81-6, OSW-1
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); NPO (Natural product occurrence); PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); RACT (Reactant or reagent); USES (Uses)
(distribution of antitumor natural product OSW-1 in ganglioside GM3-phospholipid membranes)

RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902089 CAPLUS
DOCUMENT NUMBER: 141:395754
TITLE: Preparation of orsaponin [3β, 16β, 17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1->3)-(2-O-acetyl-α-L-arabinopyranoside)] and its derivatives for their use as cancer therapeutics
INVENTOR(S): Haung, Peng; Keating, Michael J.; Jin, Zhendong
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA; University of Iowa Research Foundation
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091484	A2	20041028	WO 2004-US10676	20040407
WO 2004091484	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005004044	A1	20050106	US 2004-819479	20040407
PRIORITY APPLN. INFO.:			US 2003-460946P P	20030407

OTHER SOURCE(S): MARPAT 141:395754
GI

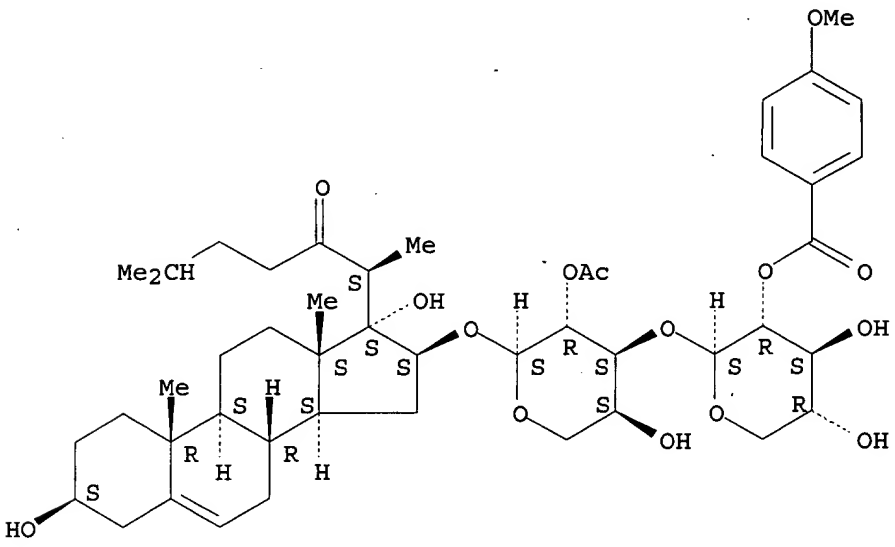
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention concerns methods for treating pancreatic cancers, leukemias, colon cancers, malignant gliomas and other brain tumors, and ovarian cancers which comprise providing to an individual compns. comprising an orsaponin or its derivs., such as I [R1 = H, OH, OMe; R2 = H, OH, ester, amide; R3, R4 = H, OH; R3R4 = double bond; R5 = H, disaccharide, monosaccharide, trisaccharide; R6 = disaccharide, monosaccharide, trisaccharide; R7, R8 = Me, alkyl; R9 = α-Me, β-Me]. The invention also provides processes and intermediates useful for preparing compds. of formula I and various therapeutically useful derivs. Thus, orsaponin (II) was prepared via a multistep reaction sequence starting from 5-pregnen-16α,17α-epoxy-3β-ol-20-one, 1,2,3,4-tetra-O-acetyl-L-arabinose, 4-methoxybenzoyl chloride and 1,2,3,4-tetra-O-acetyl-D-xylopyranose. II exhibited an IC50 = <0.1 nM in human leukemia cells (ML-1) and human lymphoma cells (Raji).

IT 145075-81-6P, Orsaponin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of orsaponin and its derivs. for their use as cancer

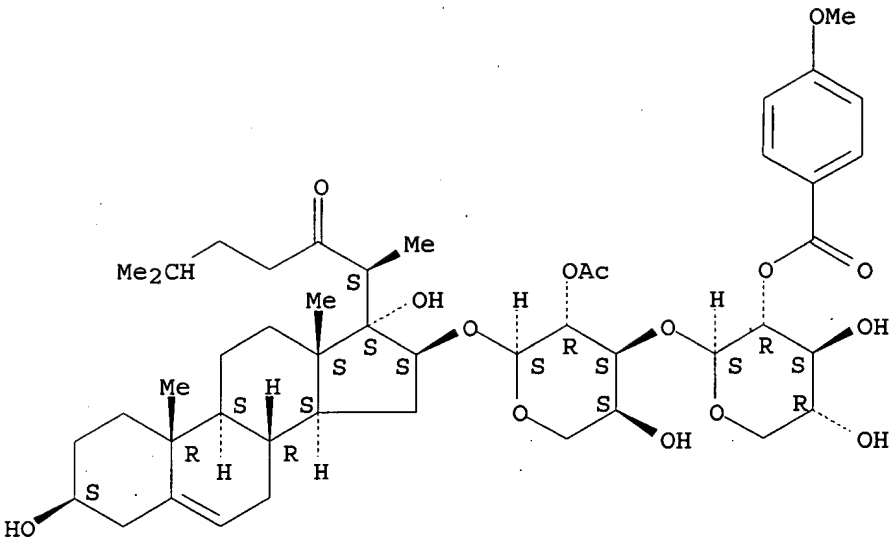
therapeutics)
RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:762999 CAPLUS
DOCUMENT NUMBER: 142:94021
TITLE: Synthesis of 5,6-dihydro-OSW-1 and its antitumor activities
AUTHOR(S): Deng, Le-Hua; Wu, Hao; Yu, Biao; Jiang, Man-Rong; Wu, Jia-Rui
CORPORATE SOURCE: State Key Laboratory of Bio-organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Chinese Journal of Chemistry (2004), 22(9), 994-998
CODEN: CJOCEV; ISSN: 1001-604X
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:94021
AB 5,6-Dihydro-OSW-1 was synthesized following our previous procedure for the total synthesis of OSW-1. This compound demonstrated slightly stronger potency than that of OSW-1 against the growth of cancer cells.
IT 145075-81-6P, Osw-1
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 5,6-dihydro-OSW-1 from 3β-hydroxyandrost-5-en-17-one and its antitumor activity)
RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

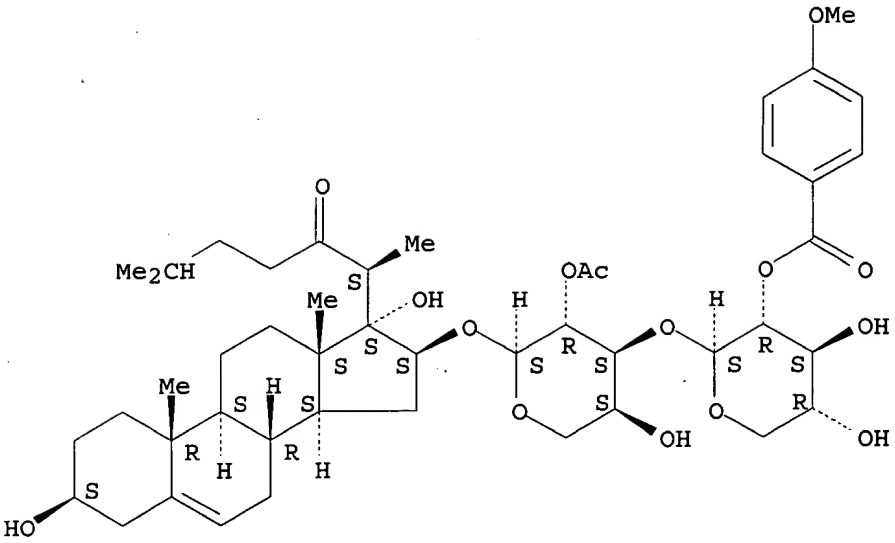
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:403914 CAPLUS
DOCUMENT NUMBER: 141:123820
TITLE: Synthesis of analogues of a potent antitumor saponin OSW-1
AUTHOR(S): Morzycki, Jacek W.; Wojtkielewicz, Agnieszka; Wolczynski, Slawomir
CORPORATE SOURCE: Institute of Chemistry, University of Bialystok, Bialystok, 15-443, Pol.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(12), 3323-3326
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:123820
AB A series of side chain analogs, a 22-glycosylated isomer, and 16β-O-L-arabinosyl or 16β-O-D-xylosyl analogs of OSW-1 were synthesized. All analogs were found to be less cytotoxic against breast and endometrial cancer cell lines than the natural product.
IT 145075-81-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. activity of analogs of potent antitumor saponin OSW-1)
RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:552629 CAPLUS
DOCUMENT NUMBER: 139:365103
TITLE: Approaches towards the synthesis of cephalostatins, ritterazines and saponins from Ornithogalum saundersiae - new natural products with cytostatic activity
AUTHOR(S): Gryszkiewicz-Wojtkielewicz, A.; Jastrzebska, I.; Morzycki, J. W.; Romanowska, D. B.
CORPORATE SOURCE: Institute of Chemistry, University of Bialystok, Bialystok, 15-443, Pol.
SOURCE: Current Organic Chemistry (2003), 7(12), 1257-1277
CODEN: CORCFE; ISSN: 1385-2728
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Secondary metabolites of marine invertebrates continue to attract the attention of organic chemists, biochemists, and pharmacologists due to their novel structures and potent biol. activities. One such example is cephalostatin 1 isolated from the Indian Ocean hemichordate Cephalodiscus gilchristi, which exhibited remarkable cytotoxic activity against a broad spectrum of malignant tumor cells. Similar marine alkaloids (e.g. ritterazine G) were found in the lipophilic extract of the tunicate Ritterella tokioka collected off the coast of Japan. These very potent compds., cephalostatins and ritterazines, belong to the large family of trisdecacyclic pyrazines, consisting of two steroid units. The two steroid halves of cephalostatin 1 and other highly cytotoxic members of the family are different. The biol. activity of the dimeric steroid-pyrazine marine alkaloids and their limited availability coupled with the new and intriguing structure make them an attractive challenge for the synthetic organic chemists. A few years ago a group of cholestane glycosides was isolated from the bulbs of Ornithogalum saundersiae, a species of the lily family without any medicinal folkloric background. Similar glycosides were recently isolated from Galtonia candicans. The major component of the mixture of saponins, OSW-1, exhibited sub-nanomolar antineoplastic activity. While OSW-1 is exceptionally cytotoxic against various tumor cells, it showed little toxicity to normal human pulmonary cells. The cytotoxicity profile of OSW-1 against different cancer cell lines was found to be surprisingly similar to that of the cephalostatins, which appears to imply a related mechanism of action. In

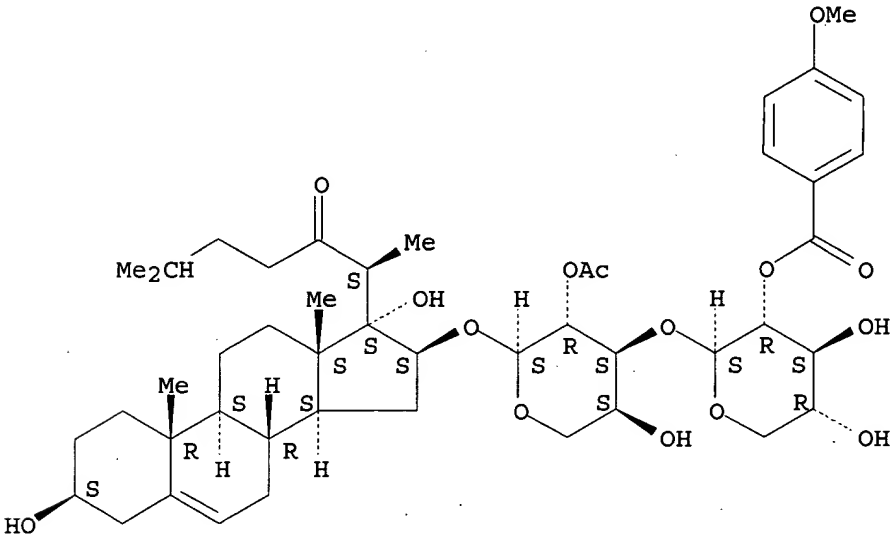
this review article the synthetic efforts towards these compds. are described.

IT 145075-81-6DP, OSW-1, analogs
RL: PNU (Preparation, unclassified); PREP (Preparation)
(review of approaches towards the synthesis of cephalostatins, ritterazines and saponins from Ornithogalum saundersiae, new natural products with cytostatic activity)

RN 145075-81-6 CAPLUS

CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:159561 CAPLUS
DOCUMENT NUMBER: 137:20496
TITLE: New natural products with cytostatic activity
AUTHOR(S): Gryszkiewicz, Agnieszka; Jastrzebska, Izabella; Morzycki, Jacek W.
CORPORATE SOURCE: Inst. Chem., Uniw. Bialystok, Bialystok, 15-443, Pol.
SOURCE: Wiadomosci Chemiczne (2001), 55(9-10), 793-820
CODEN: WICHAP; ISSN: 0043-5104
PUBLISHER: Wydawnictwo Uniwersytetu Wroclawskiego
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Polish

AB A review. Secondary metabolites of marine invertebrates continue to attract attention of organic chemists, biochemists, and pharmacologists due to their interesting structures and potent biol. activities. One such example is cephalostatin 1 isolated from the Indian Ocean hemichordate Cephalodiscus gilchristi, which exhibited remarkable cytotoxic activity against a broad spectrum of malignant tumor cells. Similar marine alkaloids (e.g. ritterazine G) were found in the lipophilic extract of the tunicate Ritterella tokioka collected off the coast of Japan. These very potent compds., cephalostatins and ritterazines, belong to the large family of trisdecacyclic pyrazines consisting of two steroid units. The two steroid halves of cephalostatin 1 and other highly cytotoxic members of the family are different. The biol. activity of the dimeric steroid-pyrazine marine alkaloids and their limited availability coupled with the new and intriguing structure make them an attractive challenge

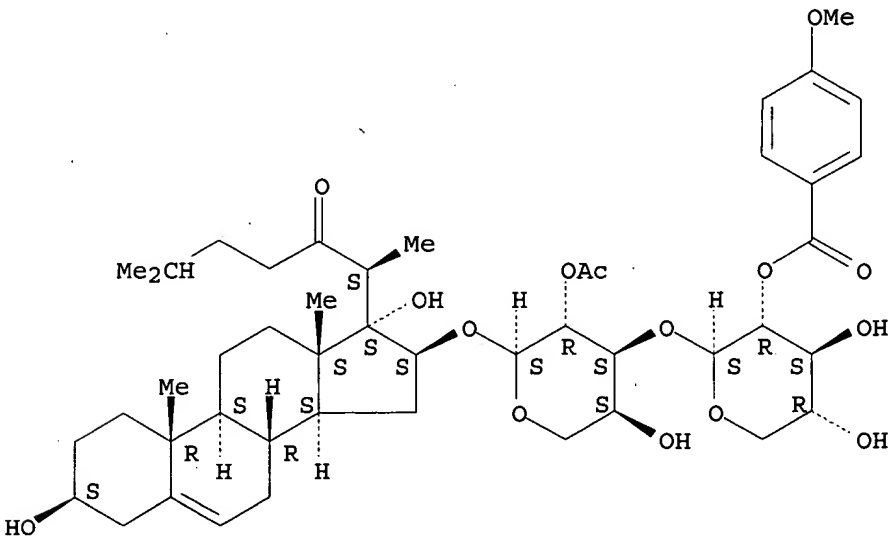
for the synthetic organic chemists. A few years ago a group of cholestane glycosides was isolated from the bulbs of Ornithogalum saundersiae, a species of the lily family without any medicinal folkloric background. The major component of the mixture of saponins, OSW-1, exhibited sub-nanomolar antineoplastic activity. While OSW-1 is exceptionally cytotoxic against various tumor cells, it showed little toxicity to normal human pulmonary cells. The cytotoxicity profile of OSW-1 against different cancer cell lines was found to be surprisingly similar to that of the cephalostatins, which appears to imply a related mechanism of action. In this review article the synthetic efforts towards these compds. are described. One of the key features of any attempted synthesis of bis-steroidal pyrazines is the central heterocyclic ring. The classical method of pyrazine synthesis involves the dimerization of a-amino ketones. An obvious disadvantage of α-amino ketones dimerizations is their unsuitability for unsym. cross-coupling. Various methods for preparation of unsym. pyrazines were developed. However, the preparation of suitably functionalized steroid units is still an uphill challenge, although a significant progress in this endeavor was achieved. This is exemplified among others by the synthesis of cephalostatin 1. The highly active "interphylal" hybrid analogs, ritterostatins and ornithostatins, were also obtained. Since saponin OSW-1 contains a relatively simple steroid skeleton, it is an attractive synthetic goal. The synthesis of the OSW-1 aglycon, and later the saponin OSW-1, was successfully accomplished. The mode of action of OSW-1 and of the cephalostatin family is not known yet, but it seems that an oxocarbenium ion, which could be generated from both types of compds., is the likely intermediate responsible for their cytotoxicity.

IT 145075-81-6P, OSW-1
RL: SPN (Synthetic preparation); PREP (Preparation)
(review of saponin natural products with cytostatic activity)

RN 145075-81-6 CAPLUS

CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 9 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2005651744 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16333034
TITLE: OSW-1: a natural compound with potent anticancer activity and a novel mechanism of action.

AUTHOR: Zhou Yan; Garcia-Prieto Celia; Carney Dennis A; Xu Rui-hua; Pelicano Helene; Kang Ying; Yu Wensheng; Lou Changgang; Kondo Seiji; Liu Jinsong; Harris David M; Estrov Zeev; Keating Michael J; Jin Zhendong; Huang Peng

CORPORATE SOURCE: Department of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA.

CONTRACT NUMBER: CA105073 (NCI)
CA109041 (NCI)
CA16672 (NCI)
CA85563 (NCI)

SOURCE: Journal of the National Cancer Institute, (2005 Dec 7) Vol. 97, No. 23, pp. 1781-5.
Journal code: 7503089. E-ISSN: 1460-2105.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200512

ENTRY DATE: Entered STN: 16 Dec 2005
Last Updated on STN: 20 Dec 2005
Entered Medline: 15 Dec 2005

AB The naturally occurring compound 3beta,16beta,17alpha-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-beta-D-xylopyranosyl)-(1-->3)-(2-O-acetyl-alpha-L-arabinopyranoside) (OSW-1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concentrations that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochemical analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro analysis revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.

L7 ANSWER 10 OF 10 MEDLINE on STN

ACCESSION NUMBER: 2004298568 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15149699

TITLE: Synthesis of analogues of a potent antitumor saponin OSW-1.

AUTHOR: Morzycki Jacek W; Wojtkielewicz Agnieszka; Wolczynski Slawomir

CORPORATE SOURCE: Institute of Chemistry, University of Bialystok, al. Pilsudskiego 11/4, 15-443 Bialystok, Poland..
morzycki@uwb.edu.pl

SOURCE: Bioorganic & medicinal chemistry letters, (2004 Jun 21) Vol. 14, No. 12, pp. 3323-6.
Journal code: 9107377. ISSN: 0960-894X.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

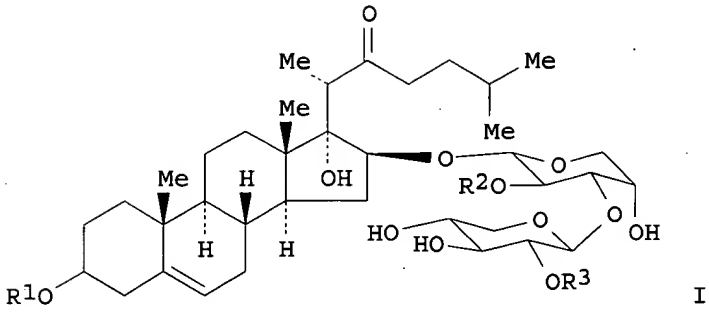
ENTRY MONTH: 200501

ENTRY DATE: Entered STN: 18 Jun 2004
Last Updated on STN: 7 Jan 2005

Entered Medline: 6 Jan 2005

AB A series of side chain analogues (5a-e), a 22-glycosylated isomer (10), and 16beta-O-l-arabinosyl (13a) or 16beta-O-d-xylosyl (13b) analogues of OSW-1 were synthesized. All analogues were found to be less cytotoxic against breast and endometrial cancer cell lines than the natural product.

L8 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:703701 CAPLUS
DOCUMENT NUMBER: 126:4640
TITLE: Cholestane glycosides from Ornithogalum saundersiae and their potent cytotoxic activity on various malignant tumor cells
AUTHOR(S): Mimaki, Yoshihiro; Kuroda, Minpei; Kameyama, Aiko; Sashida, Yutaka; Hirano, Toshihiko; Oka, Kitaro; Maekawa, Rhuji; Wada, Toru; Sugita, Kenji
CORPORATE SOURCE: School Pharmacy, Tokyo University Pharmacy and Life Science, Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1996), 38th, 313-318
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

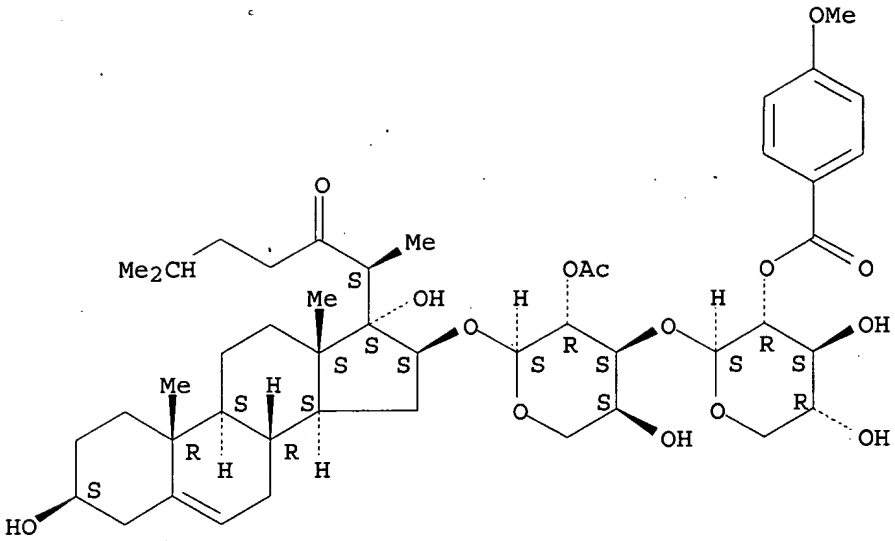
AB Seven cholestane glycosides (I: R1 = H or Glc; R2 = H or Ac; R3 = p-methoxybenzoyl, H, etc.) are isolated from hot MeOH extract of bulb of O. saundersiae, and their structures determined I have cytotoxic activities against HL-60 and human T-lymphocyte leukemia MOLT-4 cell. One of I has antitumor activity 10-100-fold higher than com. available products such as mitomycin but does not inhibit normal human pulmonary cell.

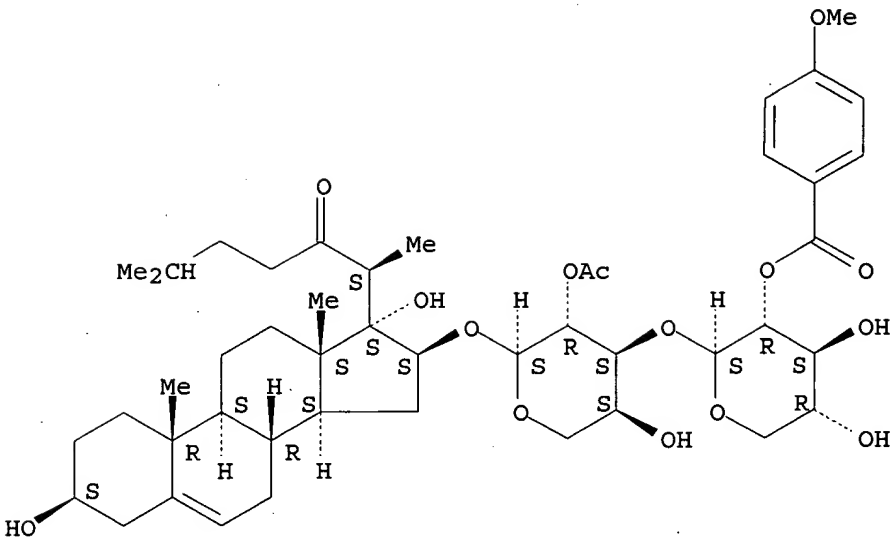
IT 145075-81-6P
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(cholestane glycosides from Ornithogalum saundersiae and potent cytotoxic activity on various malignant tumor cells)

RN 145075-81-6 CAPLUS

CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

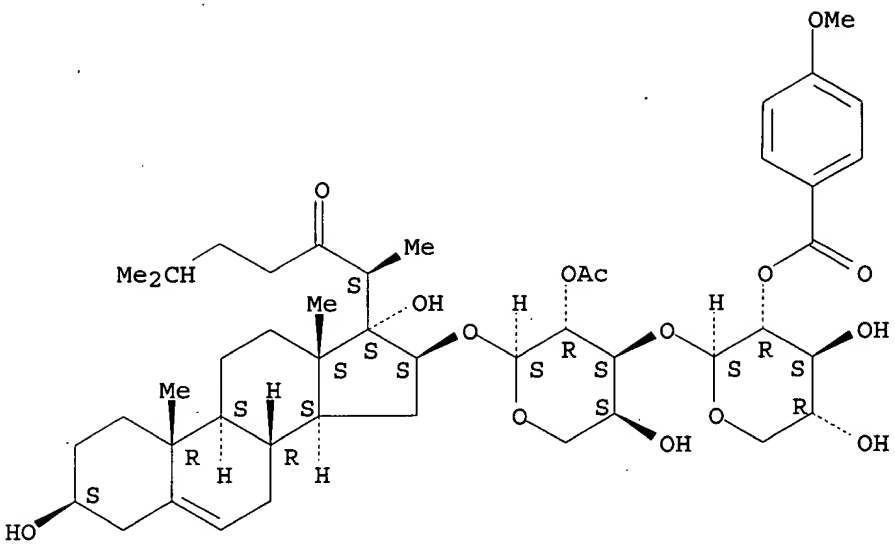
Absolute stereochemistry. Rotation (-).


OMe
O
Me
Me2CH
S
OAc
O
O
Me
OH
H
H
OH
O
S
S
S
R
S
S
R
S
Me
S
H
S
O
S
O
S
R
R
H
H
OH
OH
S
HO


OMe
O
Me
Me2CH
S
OH
OAc
H
O
Me
S
S
S
S
R
S
S
S
R
S
OH
Me
S
H
S
O
S
O
R
OH
R
H
R
H
S
HO

L8 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1300875 CAPLUS
DOCUMENT NUMBER: 144:425214
TITLE: OSW-1: a Natural Compound With Potent Anticancer Activity and a Novel Mechanism of Action
AUTHOR(S): Zhou, Yan; Garcia-Prieto, Celia; Carney, Dennis A.; Xu, Rui-Hua; Pelicano, Helene; Kang, Ying; Yu, Wensheng; Lou, Changgang; Kondo, Seiji; Liu, Jinsong; Harris, David M.; Estrov, Zeev; Keating, Michael J.; Jin, Zhendong; Huang, Peng
CORPORATE SOURCE: Departments of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of the National Cancer Institute (2005), 97(23), 1781-1785
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The naturally occurring compound 3β,16β,17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1 3)-(2-O-acetyl-α-L-arabinopyranoside) (OSW-1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concns. that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochem. analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro anal. revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.
IT 145075-81-6, OSW-1
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(OSW-1 damaged mitochondrial membrane and cristae, leading to loss of transmembrane potential, increased cytosolic calcium and activation of calcium-dependent apoptosis in both human leukemia tissue and in pancreatic cancer cell line)
RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1287404 CAPLUS
DOCUMENT NUMBER: 144:32043
TITLE: Apoptosis induced by a new member of saponin family is mediated through caspase-8-dependent cleavage of Bcl-2
AUTHOR(S): Zhu, Jianbei; Xiong, Lei; Yu, Biao; Wu, Jiarui
CORPORATE SOURCE: Laboratory of Proteomics, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, Peop. Rep. China
SOURCE: Molecular Pharmacology (2005), 68(6), 1831-1838
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB OSW-1 is a new member of cholestane saponin family, which is cytotoxic against several types of malignant cells. We reported herein that OSW-1 induced apoptosis of mammalian cells in a concentration- and time-dependent manner. The drug-induced apoptosis was mediated through the mitochondrial pathway, involving the cleavage of Bcl-2. This drug-induced Bcl-2 cleavage in Chinese hamster ovary (CHO) cells could be suppressed either by dominant-neg. caspase-8 or by a caspase-8 inhibitor, suggesting that the Bcl-2 cleavage is dependent on caspase-8. In contrast, the Bcl-2 cleavage was independent of caspase-3 activity. The inhibition of caspase-8 activity also resulted in the reduction of apoptotic cells, indicating that Bcl-2 cleavage induced by caspase-8 promotes the progression of apoptosis. The involvement of the caspase-8 activity in the processes of the OSW-1-induced apoptosis was further examined by using caspase-8-deficient Jurkat T cells. It was found that the caspase-8-deficient cells were resistant to OSW-1-induced Bcl-2 cleavage or apoptosis. Furthermore, the small subunit of caspase-8 was found to interact with Bcl-2 as determined by yeast two-hybrid and coimmunopptn. assays. Overexpression of caspase-8 small subunit reduced the cleavage of Bcl-2 and inhibited the apoptosis induced by OSW-1. Taken together, these results demonstrate that OSW-1 is capable of inducing apoptosis in mammalian cells, in which the caspase-8-dependent cleavage of Bcl-2 plays an important role.

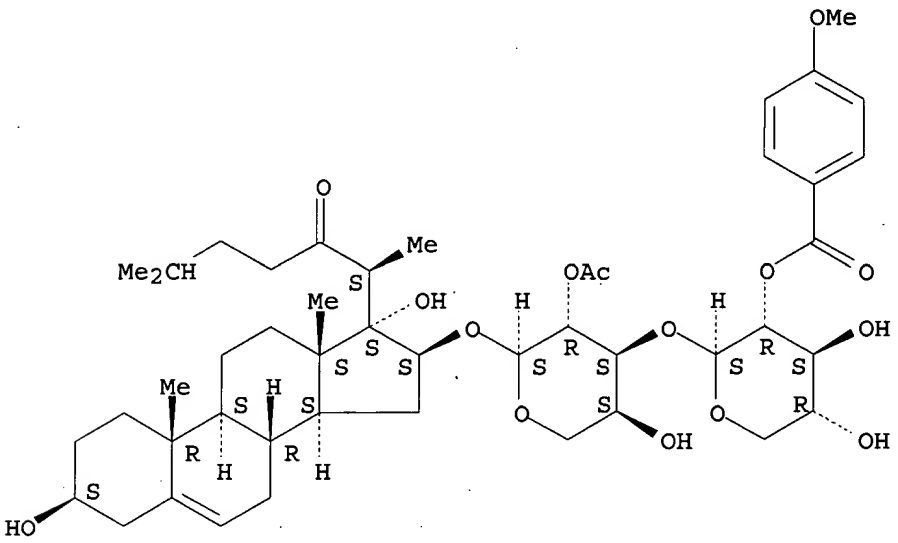
IT 145075-81-6, OSW-1
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(saponin OSW1 induction of apoptosis mediated through caspase-8-dependent cleavage of Bcl-2)

RN 145075-81-6 CAPLUS

CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:902089 CAPLUS

DOCUMENT NUMBER: 141:395754

TITLE: Preparation of orsaponin [3β, 16β, 17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1->3)-(2-O-acetyl-α-L-arabinopyranoside)] and its derivatives for their use as cancer therapeutics

INVENTOR(S): Haung, Peng; Keating, Michael J.; Jin, Zhendong

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA; University of Iowa Research Foundation

SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091484	A2	20041028	WO 2004-US10676	20040407
WO 2004091484	A3	20050909		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005004044 A1 20050106 US 2004-819479 20040407
PRIORITY APPLN. INFO.: US 2003-460946P P 20030407
OTHER SOURCE(S): MARPAT 141:395754
GI

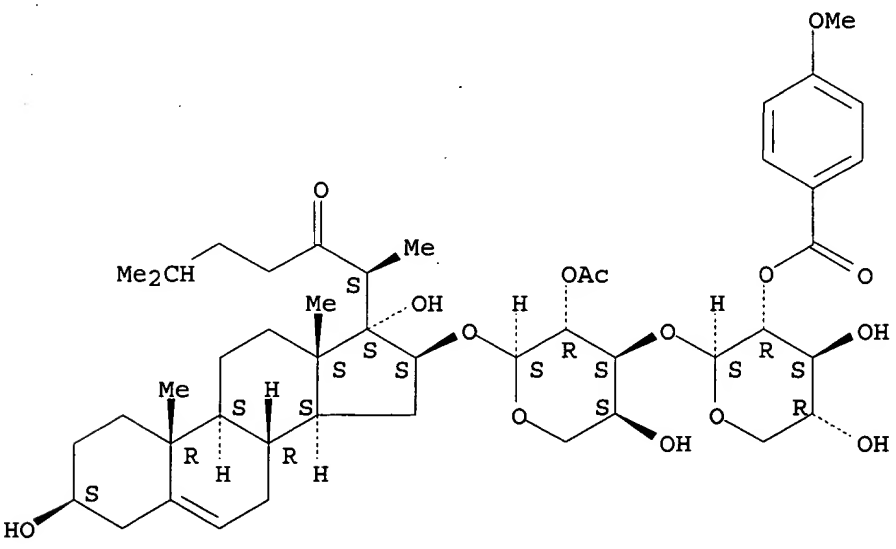
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention concerns methods for treating pancreatic cancers, leukemias, colon cancers, malignant gliomas and other brain tumors, and ovarian cancers which comprise providing to an individual compns. comprising an orsaponin or its derivs., such as I [R1 = H, OH, OMe; R2 = H, OH, ester, amide; R3, R4 = H, OH; R3R4 = double bond; R5 = H, disaccharide, monosaccharide, trisaccharide; R6 = disaccharide, monosaccharide, trisaccharide; R7, R8 = Me, alkyl; R9 = α-Me, β-Me]. The invention also provides processes and intermediates useful for preparing compds. of formula I and various therapeutically useful derivs. Thus, orsaponin (II) was prepared via a multistep reaction sequence starting from 5-pregnen-16α,17α-epoxy-3β-ol-20-one, 1,2,3,4-tetra-O-acetyl-L-arabinose, 4-methoxybenzoyl chloride and 1,2,3,4-tetra-O-acetyl-D-xylopyranose. II exhibited an IC50 = <0.1 nM in human leukemia cells (ML-1) and human lymphoma cells (Raji).

IT 145075-81-6P, Orsaponin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of orsaponin and its derivs. for their use as cancer therapeutics)

RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:613010 CAPLUS

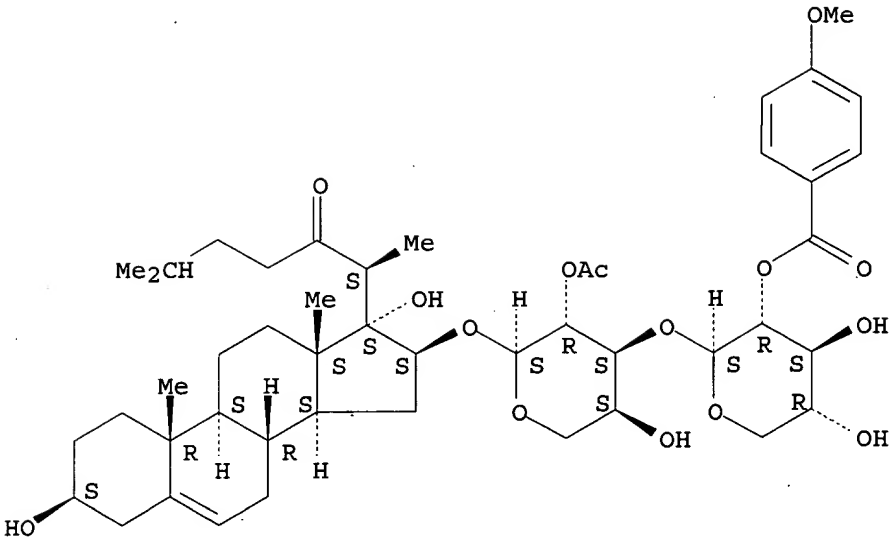
DOCUMENT NUMBER: 140:14812
TITLE: OSW-1 related compounds from the bulbs of Ornithogalum thyrsoides and their cytostatic activity on HL-60 cells
AUTHOR(S): Kuroda, Minpei; Hasegawa, Fusako; Yokosuka, Akihito; Mimaki, Yoshihiro; Sashida, Yutaka
CORPORATE SOURCE: School of Pharm., Tokyo Univ. of Pharm. and Life Sci., Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (2001), 43rd, 371-376
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB An acylated cholestane diglycoside, tentatively named OSW-1, isolated by us from the bulbs of Omithogalum saundersiae (Liliaceae), has been found to show potent cytotoxicity against a variety of tumor cell culture lines and exptl. animal tumors. During our going project focused on higher-plant antineoplastic constituents, we undertook a phytochem. investigation of the methanolic extract of Omithogalum thyrsoides Jacg. This resulted in the isolation of eleven cholestane glycosides (1-11) based upon 3β, 16β, 17α-trihydroxycholest-5-en 22-one, including eight new compds. (4-11). The structures of 4-11 were determined by spectroscopic anal., including 2D NNW spectroscopic data, and the results of acid- and alkaline catalyzed hydrolysis. The isolated compds. were evaluated for cytostatic activity on leukemia HL-60 cells. The cytostatic activity of 4 (IC50: 0.00015 μM) was as potent as that of OSW-1. The cytostatic activities of 6 and 7, having an addnl. glucosyl unit at C-6 of the terminal glucosyl moiety of 3 and 4, resp., were less potent than that of 4 by about 3 orders of magnitude. However, further glycosylation of the C-4" hydroxyl group of the terminal glucosyl moiety of 6 and 7 resulted in no discernible effects on the activity (3: 0.00048, 4: 0.00015→6: 0.66, 7: 0.56-9: 0.53, 10: 0.54 (IC50, μM)). The detailed cytostatic-structure relationships of the OSW-1 related compds. are inclusively reported.

IT 145075-81-6DP, OSW-1, derivs.
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(OSW-1 related antitumor compds. from the bulbs of Ornithogalum thyrsoides and their cytostatic activity on HL-60 cells)

RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

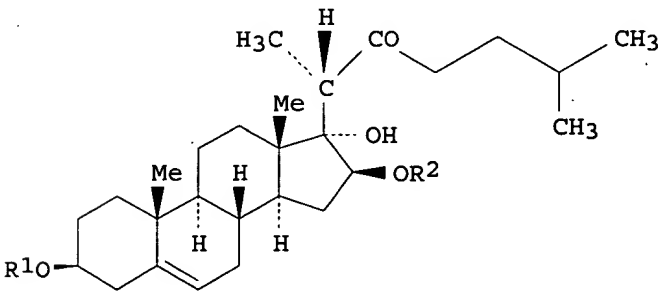
Absolute stereochemistry. Rotation (-).



L8 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:276067 CAPLUS
DOCUMENT NUMBER: 126:255476
TITLE: Steroid glycosides from Ornithogalum saundersiae for antitumor agents and immunosuppressants
INVENTOR(S): Sashita, Yutaka; Oka, Kitaro; Hirano, Toshihiko; Mimaki, Yoshihiro; Kuroda, Akihira; Fujii, Akio; Myata, Yoshuki
PATENT ASSIGNEE(S): Pola Kasei Kogyo KK, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 09048794	A2	19970218	JP 1996-109327		19960430
PRIORITY APPLN. INFO.:			JP 1995-136377	A	19950602
			JP 1995-136378	A	19950602

OTHER SOURCE(S): MARPAT 126:255476
GI



I

AB Steroid glycosides (I) [R1 = H or sugar residues with/without acyl group; R2 = sugar residues with/without acyl group] are extracted and purified from

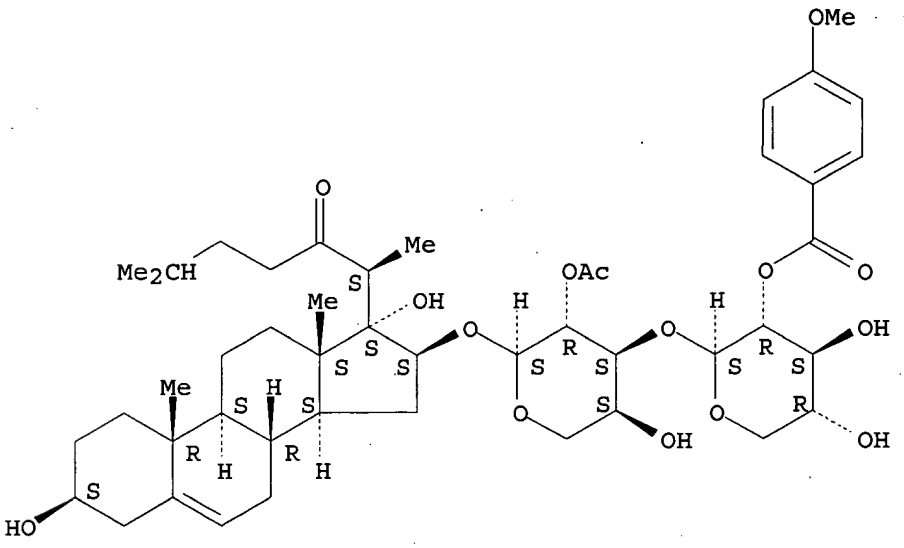
O. saundersiae for antitumor agents and immunosuppressants. I inhibited the growth of leukemia HL-60 cells in cultures with IC50 values ranging from 0.0002 to 0.25 μM. Immunosuppressant activity also was demonstrated using T cell-derived, CD receptor-containing MOLT-4 cells.

IT 145075-81-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(steroid glycosides from Ornithogalum saundersiae for antitumor agents and immunosuppressants)

RN 145075-81-6 CAPLUS

CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:188947 CAPLUS

DOCUMENT NUMBER: 126:258484

TITLE: Cholestane glycosides with potent cytostatic activities on various tumor cells from Ornithogalum saundersiae bulbs

AUTHOR(S): Mimaki, Yoshihiro; Kuroda, Minpei; Kameyama, Aiko; Sashida, Yutaka; Hirano, Toshihiko; Oka, Kitaro; Maekawa, Rhuji; Wada, Toru; Sugita, Kenji; Beutler, John A.

CORPORATE SOURCE: School of Pharmacy, Tokyo University of Pharmacy and Life Science, Tokyo, 192-03, Japan

SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(5), 633-636
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

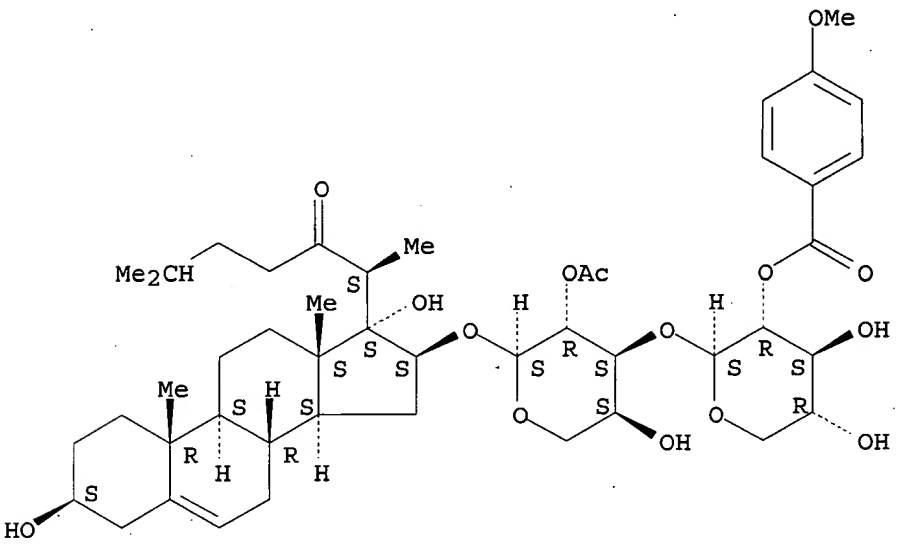
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Five cholestane glycosides, including three new ones, with potent cytostatic activity against leukemia HL-60 cells were isolated from Ornithogalum saundersiae bulbs. 3β,16β,17α-Trihydroxycholest-5-en-22-one 16-O(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)(1→3)-(2-O-acetyl-α-L-arabinopyranoside) showed exceptionally potent cytostatic activities against various malignant tumor cells such as human pulmonary carcinoma.

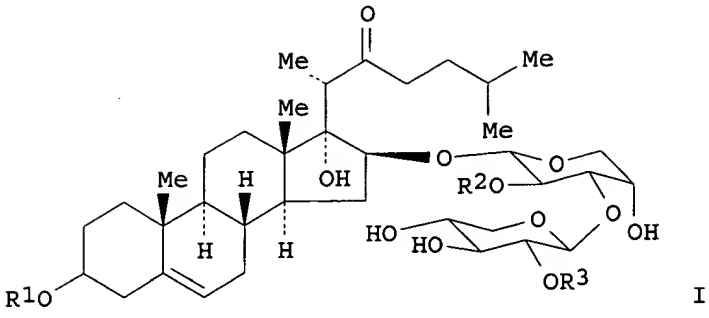
IT 145075-81-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isolation and antitumor activity of cholestane glycosides from Ornithogalum saundersiae)
RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:703701 CAPLUS
DOCUMENT NUMBER: 126:4640
TITLE: Cholestane glycosides from Ornithogalum saundersiae and their potent cytotoxic activity on various malignant tumor cells
AUTHOR(S): Mimaki, Yoshihiro; Kuroda, Minpei; Kameyama, Aiko; Sashida, Yutaka; Hirano, Toshihiko; Oka, Kitaro; Maekawa, Rhuji; Wada, Toru; Sugita, Kenji
CORPORATE SOURCE: School Pharmacy, Tokyo University Pharmacy and Life Science, Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1996), 38th, 313-318
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

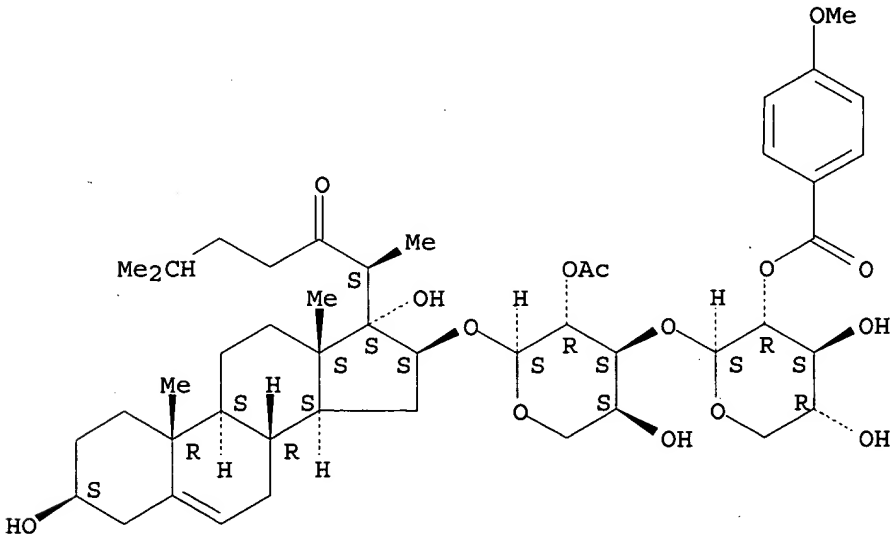
AB Seven cholestane glycosides (I: R1 = H or Glc; R2 = H or Ac; R3 = p-methoxybenzoyl, H, etc.) are isolated from hot MeOH extract of bulb of O. saundersiae, and their structures determined I have cytotoxic activities against HL-60 and human T-lymphocyte leukemia MOLT-4 cell. One of I has antitumor activity 10-100-fold higher than com. available products such as mitomycin but does not inhibit normal human pulmonary cell.

IT 145075-81-6P
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(cholestane glycosides from Ornithogalum saundersiae and potent cytotoxic activity on various malignant tumor cells)

RN 145075-81-6 CAPLUS

CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 8 OF 9 MEDLINE on STN

ACCESSION NUMBER: 2005651744 MEDLINE

DOCUMENT NUMBER: PubMed ID: 16333034

TITLE: OSW-1: a natural compound with potent anticancer activity and a novel mechanism of action.

AUTHOR: Zhou Yan; Garcia-Prieto Celia; Carney Dennis A; Xu Rui-hua; Pelicano Helene; Kang Ying; Yu Wensheng; Lou Changgang; Kondo Seiji; Liu Jinsong; Harris David M; Estrov Zeev;

Keating Michael J; Jin Zhendong; Huang Peng
CORPORATE SOURCE: Department of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA.
CONTRACT NUMBER: CA105073 (NCI)
CA109041 (NCI)
CA16672 (NCI)
CA85563 (NCI)
SOURCE: Journal of the National Cancer Institute, (2005 Dec 7) Vol. 97, No. 23, pp. 1781-5.
Journal code: 7503089. E-ISSN: 1460-2105.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 16 Dec 2005
Last Updated on STN: 20 Dec 2005
Entered Medline: 15 Dec 2005

AB The naturally occurring compound 3beta,16beta,17alpha-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-beta-D-xylopyranosyl)-(1-->3)-(2-O-acetyl-alpha-L-arabinopyranoside) (OSW-1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concentrations that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochemical analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro analysis revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.

L8 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2001467851 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11514158
TITLE: Synthesis of OSW-1 analogues and a dimer and their antitumor activities.
AUTHOR: Ma X; Yu B; Hui Y; Miao Z; Ding J
CORPORATE SOURCE: State Key Laboratory of Bio-organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 200032, Shanghai, China.
SOURCE: Bioorganic & medicinal chemistry letters, (2001 Aug 20) Vol. 11, No. 16, pp. 2153-6.
Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 30 Aug 2001
Last Updated on STN: 8 Oct 2001
Entered Medline: 4 Oct 2001

AB Five analogues, including a 16-epi-isomer (6), and a 3-terephthalic acid linked dimer (8) of OSW-1 were synthesized. Their inhibitory activities

on P388 and A-549 cells were detected.

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902089 CAPLUS
DOCUMENT NUMBER: 141:395754
TITLE: Preparation of orsaponin [3β, 16β, 17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1->3)-(2-O-acetyl-α-L-arabinopyranoside)] and its derivatives for their use as cancer therapeutics
INVENTOR(S): Haung, Peng; Keating, Michael J.; Jin, Zhendong
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA; University of Iowa Research Foundation
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091484	A2	20041028	WO 2004-US10676	20040407
WO 2004091484	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005004044	A1	20050106	US 2004-819479	20040407
PRIORITY APPLN. INFO.:			US 2003-460946P P	20030407

OTHER SOURCE(S): MARPAT 141:395754
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention concerns methods for treating pancreatic cancers, leukemias, colon cancers, malignant gliomas and other brain tumors, and ovarian cancers which comprise providing to an individual compns. comprising an orsaponin or its derivs., such as I [R1 = H, OH, OMe; R2 = H, OH, ester, amide; R3, R4 = H, OH; R3R4 = double bond; R5 = H, disaccharide, monosaccharide, trisaccharide; R6 = disaccharide, monosaccharide, trisaccharide; R7, R8 = Me, alkyl; R9 = α-Me, β-Me]. The invention also provides processes and intermediates useful for preparing compds. of formula I and various therapeutically useful derivs. Thus, orsaponin (II) was prepared via a multistep reaction sequence starting from 5-pregnen-16α,17α-epoxy-3β-ol-20-one, 1,2,3,4-tetra-O-acetyl-L-arabinose, 4-methoxybenzoyl chloride and 1,2,3,4-tetra-O-acetyl-D-xylopyranose. II exhibited an IC50 = <0.1 nM in human leukemia cells (ML-1) and human lymphoma cells (Raji).

IT 145075-81-6P, Orsaponin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of orsaponin and its derivs. for their use as cancer therapeutics)

RN 145075-81-6 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3,17-dihydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).